



COPY OF PAPERS
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SEQUENCE LISTING

<110> Bristol-Myers Squibb Company

<120> AGGRECAN DEGRADING METALLO PROTEASES

<130> DM6909B

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<170> PatentIn version 3.0

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<212> DNA

<213> Homo sapiens

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<221> CDS

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Gln Pro Cys Leu Leu Leu Pro Ile Val Pro Leu Ser Trp Leu Val Trp
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Leu Leu Leu Leu Leu Ala Ser Leu Leu Pro Ser Ala Arg Leu Ala
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TECH CENTER 1600/2900

INS
CI

B

Ser Pro Leu Pro Arg Glu Glu Glu Ile Val Phe Pro Glu Lys Leu Asn
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 Glu Leu Leu Gly Gly Ala Glu Pro Gly Thr Tyr Leu Thr Gly Thr Ile
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 aat gga gat ccg gag tcg gtg gca tct ctg cac tgg gat ggg gga gcc 849
 Asn Gly Asp Pro Glu Ser Val Ala Ser Leu His Trp Asp Gly Gly Ala
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 ctg gag gga ggc acc cct aac tct gct ggg gga cct ggg gct cac atc 945
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 Val Met Ala Ala Ala Ala Lys Ala Phe Lys His Pro Ser Ile Arg Asn
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 cct gtc agc ttg gtg gtg act cgg cta gtg atc ctg ggg tca ggc gag 1233
 Pro Val Ser Leu Val Val Thr Arg Leu Val Ile Leu Gly Ser Gly Glu
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Ser Thr Cys Asp Thr Leu Gly Met Ala Asp Val Gly Thr Val Cys Asp			
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Pro Ala Arg Ser Cys Ala Ile Val Glu Asp Asp Gly Leu Gln Ser Ala			
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Ser Pro Cys Ser Ala Arg Phe Ile Thr Asp Phe Leu Asp Asn Gly Tyr			
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Cys Met Gly Gly Arg Cys Leu His Met Asp Gln Leu Gln Asp Phe Asn			
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 Gly Ala His Ile Leu Arg Arg Lys Ser Pro Ala Ser Gly Gln Gly Pro

INS
 CI

INS
C1

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 Gly Arg Arg Thr Arg Phe Arg Ser Cys Asn Thr Glu Asp Cys Pro Thr
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 Val Leu Val Ala Gly Asn Pro Gln Asp Thr Arg Leu Arg Tyr Ser Phe

INS
C1

785 790 795 800

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Met Leu Leu Gly Trp Ala Ser Leu Leu Leu Cys Ala Phe Arg Leu Pro
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Gln Pro Pro Thr Ala Ala Ala Ala Ala Gln Pro Arg Arg Arg Gln Gly
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gcg cag cgg cgc agg agc aag ggg ctg gtg cag aac atc gac caa ctc 360

INS
C1

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 100 105 110

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 His Cys Phe Tyr Arg Gly Thr Val Asp Ala Ser Pro Arg Ser Leu Ala
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gaa aag ggg cgc gtg tac ggg gat ggg tcc gca cgg atc ctg cac gtc 696
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tgc gaa acc ccc gcg tcc aca ccg gag gcc cac gag cat gct ccg gcg 792
 Cys Glu Thr Pro Ala Ser Thr Pro Glu Ala His Glu His Ala Pro Ala
 210 215 220

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 Gln Ser Ala Leu Ser Pro Ala Gly Gly Ser Gly Pro Gln Thr Trp Trp
 245 250 255

cgg cgg cgg cgc cgc tcc atc tcc ccg gcc cgc cag gtg gag ctg ctt 936
 Arg Arg Arg Arg Arg Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu
 260 265 270

ctg gtg gct gac gcg tcc atg gcg ccg ttg tat ggc cgg ggc ctg cag 984
 Leu Val Ala Asp Ala Ser Met Ala Arg Leu Tyr Gly Arg Gly Leu Gln
 275 280 285

cat tac ctg ctg acc ctg gcc tcc atc gcc aat agg ctg tac agc cat 1032
 His Tyr Leu Leu Thr Leu Ala Ser Ile Ala Asn Arg Leu Tyr Ser His

INS
C1

290 295 300

gct agc atc gag aac cac atc cgc ctg gcc gtg gtg aag gtg gtg gtg 1080
Ala Ser Ile Glu Asn His Ile Arg Leu Ala Val Val Lys Val Val Val
305 310 315 320

cta ggc gac aag gac aag agc ctg gaa gtg agc aag aac gct gcc acc 1128
Leu Gly Asp Lys Asp Lys Ser Leu Glu Val Ser Lys Asn Ala Ala Thr
325 330 335

aca ctc aag aac ttt tgc aag tgg cag cac caa cac aac cag ctg gga 1176
Thr Leu Lys Asn Phe Cys Lys Trp Gln His Gln His Asn Gln Leu Gly
340 345 350

gat gac cat gag gag cac tac gat gca gct atc ctg ttt act cgg gag 1224
Asp Asp His Glu Glu His Tyr Asp Ala Ala Ile Leu Phe Thr Arg Glu
355 360 365

gat tta tgt ggg cat cat tca tgt gac acc ctg gga atg gca gac gtt 1272
Asp Leu Cys Gly His His Ser Cys Asp Thr Leu Gly Met Ala Asp Val
370 375 380

ggg acc ata tgt tct cca gag cgc agc tgt gct gtg att gaa gac gat 1320
Gly Thr Ile Cys Ser Pro Glu Arg Ser Cys Ala Val Ile Glu Asp Asp
385 390 395 400

ggc ctc cac gca gcc ttc act gtg gct cac gaa atc gga cat tta ctt 1368
Gly Leu His Ala Ala Phe Thr Val Ala His Glu Ile Gly His Leu Leu
405 410 415

ggc ctc tcc cat gac gat tcc aaa ttc tgt gaa gag acc ttt ggt tcc 1416
Gly Leu Ser His Asp Asp Ser Lys Phe Cys Glu Glu Thr Phe Gly Ser
420 425 430

aca gaa gat aag cgc tta atg tct tcc atc ctt acc agc att gat gca 1464
Thr Glu Asp Lys Arg Leu Met Ser Ser Ile Leu Thr Ser Ile Asp Ala
435 440 445

tct aag ccc tgg tcc aaa tgc act tca gcc acc atc aca gaa ttc ctg 1512
Ser Lys Pro Trp Ser Lys Cys Thr Ser Ala Thr Ile Thr Glu Phe Leu
450 455 460

gat gat ggc cat ggt aac tgt ttg ctg gac cta cca cga aag cag atc 1560
Asp Asp Gly His Gly Asn Cys Leu Leu Asp Leu Pro Arg Lys Gln Ile
465 470 475 480

ctg ggc ccc gaa gaa ctc cca gga cag acc tac gat gcc acc cag cag 1608
Leu Gly Pro Glu Glu Leu Pro Gly Gln Thr Tyr Asp Ala Thr Gln Gln
485 490 495

tgc aac ctg aca ttc ggg cct gag tac tcc gtg tgt ccc ggc atg gat 1656
Cys Asn Leu Thr Phe Gly Pro Glu Tyr Ser Val Cys Pro Gly Met Asp
500 505 510

gtc tgt gct cgc ctg tgg tgt gct gtg gta cgc cag ggc cag atg gtc 1704
Val Cys Ala Arg Leu Trp Cys Ala Val Val Arg Gln Gly Gln Met Val
515 520 525

INS
CI

1752
tgt ctg acc aag aag ctg cct gcg gtg gaa ggg acg cct tgt gga aag
Cys Leu Thr Lys Lys Leu Pro Ala Val Glu Gly Thr Pro Cys Gly Lys
530 535 540

1800
ggg aga atc tgc ctg cag ggc aaa tgt gtg gac aaa acc aag aaa aaa
Gly Arg Ile Cys Leu Gln Gly Lys Cys Val Asp Lys Thr Lys Lys Lys
545 550 555 560

1848
tat tat tca acg tca agc cat ggc aac tgg gga tct tgg gga tcc tgg
Tyr Tyr Ser Thr Ser Ser His Gly Asn Trp Gly Ser Trp Gly Ser Trp
565 570 575

1896
ggc cag tgt tct cgc tca tgt gga gga gga gtg cag ttt gcc tat cgt
Gly Gln Cys Ser Arg Ser Cys Gly Gly Val Gln Phe Ala Tyr Arg
580 585 590

1944
cac tgt aat aac cct gct ccc aga aac aac gga cgc tac tgc aca ggg
His Cys Asn Asn Pro Ala Pro Arg Asn Asn Gly Arg Tyr Cys Thr Gly
595 600 605

1992
aag agg gcc atc tac cgc tcc tgc agt ctc atg ccc tgc cca ccc aat
Lys Arg Ala Ile Tyr Arg Ser Cys Ser Leu Met Pro Cys Pro Pro Asn
610 615 620

2040
ggt aaa tca ttt cgt cat gaa cag tgt gag gcc aaa aat ggc tat cag
Gly Lys Ser Phe Arg His Glu Gln Cys Glu Ala Lys Asn Gly Tyr Gln
625 630 635 640

2088
tct gat gca aaa gga gtc aaa act ttt gtg gaa tgg gtt ccc aaa tat
Ser Asp Ala Lys Gly Val Lys Thr Phe Val Glu Trp Val Pro Lys Tyr
645 650 655

2136
gca ggt gtc ctg cca gcg gat gtg tgc aag ctg acc tgc aga gcc aag
Ala Gly Val Leu Pro Ala Asp Val Cys Lys Leu Thr Cys Arg Ala Lys
660 665 670

2184
ggc act ggc tac tat gtg gta ttt tct cca aag gtg acc gat ggc act
Gly Thr Gly Tyr Tyr Val Val Phe Ser Pro Lys Val Thr Asp Gly Thr
675 680 685

2232
gaa tgt agg ccg tac agt aat tcc gtc tgc gtc cgg ggg aag tgt gtg
Glu Cys Arg Pro Tyr Ser Asn Ser Val Cys Val Arg Gly Lys Cys Val
690 695 700

2280
aga act ggc tgt gac ggc atc att ggc tca aag ctg cag tat gac aag
Arg Thr Gly Cys Asp Gly Ile Ile Gly Ser Lys Leu Gln Tyr Asp Lys
705 710 715 720

2328
tgc gga gta tgt gga gga gac aac tcc agc tgt aca aag att gtt gga
Cys Gly Val Cys Gly Gly Asp Asn Ser Ser Cys Thr Lys Ile Val Gly
725 730 735

2376
acc ttt aat aag aaa agt aag ggt tac act gac gtg gtg agg att cct
Thr Phe Asn Lys Lys Ser Lys Gly Tyr Thr Asp Val Val Arg Ile Pro
740 745 750

INS
C1

gaa ggg gca acc cac ata aaa gtt cga cag ttc aaa gcc aaa gac cag 2424
 Glu Gly Ala Thr His Ile Lys Val Arg Gln Phe Lys Ala Lys Asp Gln
 755 760 765
 act aga ttc act gcc tat tta gcc ctg aaa aag aaa aac ggt gag tac 2472
 Thr Arg Phe Thr Ala Tyr Leu Ala Leu Lys Lys Lys Asn Gly Glu Tyr
 770 775 780
 ctt atc aat gga aag tac atg atc tcc act tca gag act atc att gac 2520
 Leu Ile Asn Gly Lys Tyr Met Ile Ser Thr Ser Glu Thr Ile Ile Asp
 785 790 795 800
 atc aat gga aca gtc atg aac tat agc ggt tgg agc cac agg gat gac 2568
 Ile Asn Gly Thr Val Met Asn Tyr Ser Gly Trp Ser His Arg Asp Asp
 805 810 815
 ttc ctg cat ggc atg ggc tac tct gcc acg aag gaa att cta ata gtg 2616
 Phe Leu His Gly Met Gly Tyr Ser Ala Thr Lys Glu Ile Leu Ile Val
 820 825 830
 cag att ctt gca aca gac ccc act aaa cca tta gat gtc cgt tat agc 2664
 Gln Ile Leu Ala Thr Asp Pro Thr Lys Pro Leu Asp Val Arg Tyr Ser
 835 840 845
 ttt ttt gtt ccc aag aag tcc act cca aaa gta aac tct gtc act agt 2712
 Phe Phe Val Pro Lys Lys Ser Thr Pro Lys Val Asn Ser Val Thr Ser
 850 855 860
 cat ggc agc aat aaa gtg gga tca cac act tcg cag ccg cag tgg gtc 2760
 His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln Trp Val
 865 870 875 880
 acg ggc cca tgg ctc gcc tgc tct agg acc tgt gac aca ggt tgg cac 2808
 Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly Trp His
 885 890 895
 acc aga acg gtg cag tgc cag gat gga aac cgg aag tta gca aaa gga 2856
 Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala Lys Gly
 900 905 910
 tgt cct ctc tcc caa agg cct tct gcg ttt aag caa tgc ttg ttg aag 2904
 Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu Leu Lys
 915 920 925
 aaa tgt tagcctgtgg ttatgatctt atgcacaaag ataactggag gattcagcac 2960
 Lys Cys
 930
 cgatgcagtc gtggtgaaca ggagggtctac ctaacgcaca gaaagtcattg cttcagtgac 3020
 attgtcaaca ggagtccaat tatgggcaga atctgtcttc tgtgaccaa agaggatgtg 3080
 cactgcttca cgtgacagtg gtgaccttgc aatatagaaa aacttggggag ttattgaaca 3140
 tcccctggga ttacaagaaa cactgatgaa tgtaaataca ggggacattt gaagatggca 3200
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INS
C1

<210> 15

<211> 930

<212> PRT

<213> Homo sapiens

<400> 15

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Leu Ala Ala Val Gly Pro Ala Ala Thr Pro Ala Gln Asp Lys Ala Gly
20 25 30

Gln Pro Pro Thr Ala Ala Ala Ala Ala Gln Pro Arg Arg Arg Gln Gly
35 40 45

Glu Glu Val Gln Glu Arg Ala Glu Pro Pro Gly His Pro His Pro Leu
50 55 60

Ala Gln Arg Arg Arg Ser Lys Gly Leu Val Gln Asn Ile Asp Gln Leu
65 70 75 80

Tyr Ser Gly Gly Gly Lys Val Gly Tyr Leu Val Tyr Ala Gly Gly Arg
85 90 95

Arg Phe Leu Leu Asp Leu Glu Arg Asp Gly Ser Val Gly Ile Ala Gly
100 105 110

Phe Val Pro Ala Gly Gly Gly Thr Ser Ala Pro Trp Arg His Arg Ser
115 120 125

His Cys Phe Tyr Arg Gly Thr Val Asp Ala Ser Pro Arg Ser Leu Ala
130 135 140

Val Phe Asp Leu Cys Gly Gly Leu Asp Gly Phe Phe Ala Val Lys His
145 150 155 160

Ala Arg Tyr Thr Leu Lys Pro Leu Leu Arg Gly Pro Trp Ala Glu Glu
165 170 175

Glu Lys Gly Arg Val Tyr Gly Asp Gly Ser Ala Arg Ile Leu His Val
180 185 190

Tyr Thr Arg Glu Gly Phe Ser Phe Glu Ala Leu Pro Pro Arg Ala Ser
195 200 205

Cys Glu Thr Pro Ala Ser Thr Pro Glu Ala His Glu His Ala Pro Ala
210 215 220

His Ser Asn Pro Ser Gly Arg Ala Ala Leu Ala Ser Gln Leu Leu Asp
225 230 235 240

Gln Ser Ala Leu Ser Pro Ala Gly Gly Ser Gly Pro Gln Thr Trp Trp

				245					250					255		
Arg	Arg	Arg	Arg	Arg	Ser	Ile	Ser	Arg	Ala	Arg	Gln	Val	Glu	Leu	Leu	
			260					265					270			
Leu	Val	Ala	Asp	Ala	Ser	Met	Ala	Arg	Leu	Tyr	Gly	Arg	Gly	Leu	Gln	
		275					280					285				
His	Tyr	Leu	Leu	Thr	Leu	Ala	Ser	Ile	Ala	Asn	Arg	Leu	Tyr	Ser	His	
	290					295					300					
Ala	Ser	Ile	Glu	Asn	His	Ile	Arg	Leu	Ala	Val	Val	Lys	Val	Val	Val	
305					310					315					320	
Leu	Gly	Asp	Lys	Asp	Lys	Ser	Leu	Glu	Val	Ser	Lys	Asn	Ala	Ala	Thr	
			325						330					335		
Thr	Leu	Lys	Asn	Phe	Cys	Lys	Trp	Gln	His	Gln	His	Asn	Gln	Leu	Gly	
			340					345					350			
Asp	Asp	His	Glu	Glu	His	Tyr	Asp	Ala	Ala	Ile	Leu	Phe	Thr	Arg	Glu	
	355						360					365				
Asp	Leu	Cys	Gly	His	His	Ser	Cys	Asp	Thr	Leu	Gly	Met	Ala	Asp	Val	
370						375					380					
Gly	Thr	Ile	Cys	Ser	Pro	Glu	Arg	Ser	Cys	Ala	Val	Ile	Glu	Asp	Asp	
385					390					395					400	
Gly	Leu	His	Ala	Ala	Phe	Thr	Val	Ala	His	Glu	Ile	Gly	His	Leu	Leu	
			405						410					415		
Gly	Leu	Ser	His	Asp	Asp	Ser	Lys	Phe	Cys	Glu	Glu	Thr	Phe	Gly	Ser	
			420					425					430			
Thr	Glu	Asp	Lys	Arg	Leu	Met	Ser	Ser	Ile	Leu	Thr	Ser	Ile	Asp	Ala	
	435						440					445				
Ser	Lys	Pro	Trp	Ser	Lys	Cys	Thr	Ser	Ala	Thr	Ile	Thr	Glu	Phe	Leu	
450						455					460					
Asp	Asp	Gly	His	Gly	Asn	Cys	Leu	Leu	Asp	Leu	Pro	Arg	Lys	Gln	Ile	
465					470					475					480	
Leu	Gly	Pro	Glu	Glu	Leu	Pro	Gly	Gln	Thr	Tyr	Asp	Ala	Thr	Gln	Gln	
			485					490						495		
Cys	Asn	Leu	Thr	Phe	Gly	Pro	Glu	Tyr	Ser	Val	Cys	Pro	Gly	Met	Asp	
			500					505					510			
Val	Cys	Ala	Arg	Leu	Trp	Cys	Ala	Val	Val	Arg	Gln	Gly	Gln	Met	Val	
	515						520				525					
Cys	Leu	Thr	Lys	Lys	Leu	Pro	Ala	Val	Glu	Gly	Thr	Pro	Cys	Gly	Lys	
530						535					540					
Gly	Arg	Ile	Cys	Leu	Gln	Gly	Lys	Cys	Val	Asp	Lys	Thr	Lys	Lys	Lys	

850 855 860
 His Gly Ser Asn Lys Val Gly Ser His Thr Ser Gln Pro Gln Trp Val
 865 870 875 880
 Thr Gly Pro Trp Leu Ala Cys Ser Arg Thr Cys Asp Thr Gly Trp His
 885 890 895
 Thr Arg Thr Val Gln Cys Gln Asp Gly Asn Arg Lys Leu Ala Lys Gly
 900 905 910
 Cys Pro Leu Ser Gln Arg Pro Ser Ala Phe Lys Gln Cys Leu Leu Lys
 915 920 925
 Lys Cys
 930

<210> 16

<211> 42

<212> PRT

<213> Homo sapiens

<400> 16

Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu Leu Val Ala Asp Ala
 1 5 10 15

Ser Met Ala Arg Met Tyr Gly Arg Gly Leu Gln His Tyr Leu Leu Thr
 20 25 30

Leu Ala Ser Ile Ala Asn Lys Leu Tyr Phe
 35 40

<210> 17

<211> 23

<212> DNA

<213> Mus musculus

<400> 17

cggccacgac cctcaagaac ttt

23

<210> 18

<211> 25

<212> DNA

<213> Mus musculus

<400> 18

gcatggaggc catcatcttc aatca

25

INS
CI

<210> 19

<211> 22

<212> DNA

<213> Homo sapiens

<400> 19

gggaggattt atgtgggcat ca

22

<210> 20

<211> 23

<212> DNA

<213> Homo sapiens

<400> 20

gtgcatttgg accagggcctt aga

23

<210> 21

<211> 13

<212> PRT

<213> artificial

<220>

<223> Synthesized peptide.

<220>

<221> MOD_RES

<222> (12)..(12)

<223> Acp

<400> 21

Ser Ile Ser Arg Ala Arg Gln Val Glu Leu Leu Xaa Cys

1

5

10

INS
CI